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High Level Autoreactive IgE Serves as an Important Indicator in Lupus Nephritis

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Objective: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease characterized by the loss of immune tolerance to self-antigens, dysregulated autoantibody production, and multiple clinical manifestations. Recently, the autoreactive IgE has been found to play a functional role in amplifying loss of self-tolerance through basophil-mediated autoantibody production in SLE, and the overall levels of IgE autoantibodies may serve as indicators of active disease. Therefore, we are going to study the IgE levels in lupus nephritis (LN) patients.
Methods: We measured the C3, C4, ANA, ds-DNA and IgE levels in 157 biopsy-proven LN patients in our center, and descriptive analysis was used to study the prevalence of IgE in LN patients. Data were presented as mean ± SD.
Results: Approximately 38% (60/157) of all LN subjects studied have a higher level of IgE (>100 ng/ml), ranging from 106.0 ng/ml to over 5000 ng/ml (736.4 ± 1081.0 ng/ml). The mean age of the 60 subjects are 36.7 ± 14.0 years. Among the 60 patients, the average titer of ANA is 223.7 ± 149.5, and more than 50% presented with hypocomplementemia [C3 50.4 ± 24.3 mg/L (61.7%); C4 9.2 ± 5.9 mg/L (55%); C3+C4 (51.7%)]. Twenty-two (37.7%) of the 60 LN subjects were positive for anti-dsDNA.
Conclusion: These results indicate that increasing IgE levels in LN patients is very common, and IgE plays an important role in LN.

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0325

Frequency of $CD4^+Foxp3^+$ Treg Cells Increase But is Unable to Control Nephritis in Lupus Prone Mice

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Background: $CD4^+Foxp3^+$ regulatory T cells (Treg) play a crucial role in the maintenance of immune tolerance and prevention of autoimmune diseases. Although $Foxp3^+$ Treg has been studied for many years in lupus, the exact role of these Treg cells in lupus, particularly in lupus nephritis remains unclear.
Methods: The frequencies and numbers of $CD4^+Foxp3(GFP)^+$T cells were detected in spleens, inguinal lymph nodes, thymi and blood in New Zealand mixed (NZM) 2328 Foxp3(GFP) knock-in reporter mice at different ages, and the Treg marker such as Helios and Neuropilin-1 were measured accordingly. The suppression function of Treg from spleen of young and old lupus was tested. The serum IgG, proteinuria and renal pathology were assessed. Additionally, Treg cells were adoptively transferred to lupus mice to assess *in vivo* effects on autoantibody and lupus nephritis.
Results: The prevalence of Treg increased in spleens, inguinal lymph nodes and blood with the development of lupus nephritis, but decreased in thymi. The $Neuropilin\text{-}1^+$ Treg cells were significantly increased in lined with lupus nephritis disease, but frequencies of $Helios^+$ Treg cells remained unchanged. Treg isolated from young lupus mice can suppress the proliferation of $CD4^+$ effector T cells in vitro, but defective in Treg from old lupus mice. Autoantibody was decreased in old lupus mice by transfer of Treg from young mice; however improvement of kidney disease was not observed.
Conclusion: Our data implicate that increased Treg frequency could originate from the expansion of natural Treg subset while lupus disease progresses. Treg expansion may reflect the feedback mechanism that tries to block the lupus disease development. Nonetheless, the T or B effector cells after lupus is established may be resistant from Treg function, thus, lack of therapeutic invention with Treg cells alone could not prevent the lupus nephritis development.

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Clinical Characteristics of Lupus Nephritis Patients Suffering Acute Kidney Injury

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Objective: We assessed clinicopathologic characteristics, treatment, curative effect and prognosis of acute kidney injury (AKI) in a cohort of Chinese patients with lupus nephritis (LN).
Methods: One hundred and sixty-one patients with renal biopsy-proven lupus nephritis diagnosed between Mar 2008 and May 2014 in our center were included into analysis; 69 cases (42.9%) were identified as AKI. The clinical, laboratory, renal histopathological and prognosis data were retrospectively collected and compared between lupus nephritis patients with AKI (n = 69) and without AKI (n = 92).
Results: In comparison with the non-AKI group, patients with AKI had significantly lower baseline renal function, lower seurm albumin level and lower complement C3 level ($p < 0.05$); the proportion of Type IV LN, Acute Activity Index, cell proliferation, crescents, leukocyte infiltration, interstitial inflammatory cell infiltration, tubular atrophy, interstitial fibrosis and level of immunofluorescence C1q deposition in AKI group were higher ($p < 0.05$). Immunofluorescence C1q deposition was an independent risk factor for prognosis in AKI group (HR = 4.574, 95% CI 1.507—13.883, $p < 0.05$) and AKI was an independent risk factor affecting the efficacy of LN (HR = 2.070, 95% confidence interval 1.114—3.846, $p < 0.05$).
Conclusion: AKI is common in lupus nephritis and is an independent risk factor for prognosis.

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0368

Heat-aggregated Gamma Globulins Suppress Autophagy and Induce Injuries in Glomerular Endothelial Cells

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Background: Lupus nephritis is a common and severe complication of systemic lupus erythematosus characterized by renal function impairment. Immune complex plays an important role in disease pathogenesis and organ injury. However, the precise mechanism by which immune complex leads to organ injury is still unknown. Glomerular filtration barrier (GFB) is the structural foundation of renal function and glomerular endothelial cell (GEC) is one of the three components of GFB. As autophagy is a conserved metabolic process and shows protective role in many cell types and biologic processes, we hypothesize that immune complex may suppress autophagy in GECs and participate in endothelial cell injuries and dysfunction.
Methods: We used heat-aggregated gamma globulin (HAGG) to substitute immune complex. Monomeric IgG was used as negative control. GECs were incubated with different concentrations of HAGG and collected at different time periods. Protein related to autophagy, including LC3, p62, mTOR, p70s6k, 4E-BP-1, were measured by western blotting. Cell viability and eNOS expression were detected to evaluate endothelial cell functions. Autophagy regulators were used to investigate the role of autophagy in endothelial cell injury.
Results: HAGG led to reduced ratio of LC3 II/I and increased p62 expression in GECs. Elevated expressions of p-mTOR and its substrates p-4E-BP-1 and p-p70s6k were detected. Autophagy inducer, rapamycin, could increase p-eNOS expression in GECs, while HAGG stimulation alleviated such increase. Rapamycin slightly decreased cell number, while co-incubated with HAGG further decreased cell number.
Conclusion: Our results implied that HAGG suppressed autophagy in GECs through the mTOR-dependent pathway. HAGG decreased cell viability and eNOS expression in GECs. Suppressed autophagy induced by HAGG may provide new insights in explaining the mechanism of renal impairment in lupus nephritis.

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